17.0 HEART DISEASE AND EMF EXPOSURE: EVIDENCE

STATEMENT TO THE PUBLIC

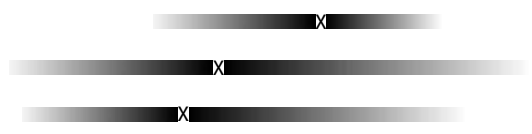
Heart disease

The reviewers used two distinct sets of guidelines to evaluate the evidence:

- *Using the guidelines that the International Agency for Research on Cancer uses to assess cancer risks, they considered the evidence as "inadequate" to implicate EMFs. This is the same conclusion reached by the workgroup of the National Institutes of Environmental Health Sciences in 1998*
- *Using the Guidelines developed especially for the California EMF Program, one of the reviewers was "close to the dividing line between believing and not believing" and two were "prone not to believe" that exposure to EMFs at home or work increases the risk of heart attack to any degree.*

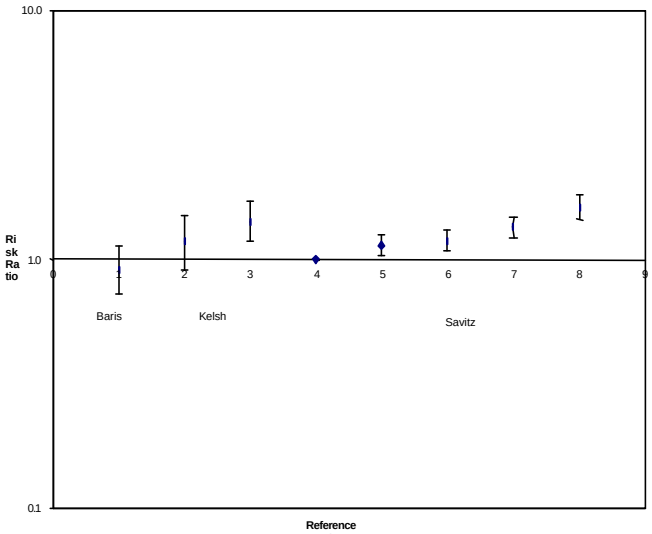
They graphed their degree of certainty as follows:

CONDITION	REVIE-WER	IARC CLASS	CERTAINTY PHRASE	DEGREE OF CERTAINTY FOR POLICY ANALYSIS THAT AN AGENT (EMFs) INCREASES DISEASE RISK TO SOME DEGREE
Heart				0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
	1	3	Close to dividing line	
	2	3	Prone not to believe	
	3	3	Prone not to believe	



17.1 THE PATTERN OF EPIDEMIOLOGICAL EVIDENCE

Figure 17.1.1 Heart Disease



There are three occupational studies that are relevant to this association. The relative risks reported in these studies are shown in Figure 17.1, the key for which is presented in Table 17.1. More details about the studies are given in Table 17.1.1. The study by Baris (Baris et al., 1996a) compared cardiovascular mortality in persons with exposures above and below the median magnetic field, electrical field and pulsed electrical exposures. No excess risk was demonstrated. Kelsh (Kelsh, 1997) examined cardiovascular mortality in broad job categories. Although non-administrative categories showed modest increases of risk relative to those of the administrative group, the categories containing jobs with the highest exposures did not show the highest relative risks. The third study by Savitz (Savitz et al., 1999) focused on deaths due to arrhythmia and acute myocardial infarction, a subgroup that was hypothesized to be vulnerable to interference in autonomic control of heart rate. A study by Sastre (Sastre, Cook & Graham, 1998) had suggested that EMFs might influence heart rate variability, and Tsuji (Tsuji et al., 1996) had demonstrated higher incidence of myocardial infarction in those with lower heart rate variability in the Framingham cohort. The Savitz (Savitz et al., 1999) study showed an association between length of employment in high-exposure jobs and estimated microtesla–years (μT-yrs) of exposure for this subgroup, but not from more chronic forms of cardiovascular disease resulting in death. These are modest but very precise associations. Two out of three studies with odds ratios above 1.0 could have easily occurred by chance. The discussion of these three studies and their impact on degree of certainty follows.

TABLE 17.1 KEY TO THE FIGURE

STUDY	EXPOSURE DEFINITION	REFERENCE NUMBER	INDIVIDUAL ODDS RATIO, MEAN	LOWER CL	UPPER CL
(Baris et al., 1996a)	< 0.16 μT vs. > 0.16 μT	1	0.91	0.73	1.14
(Kelsh, 1997)	Management & professional	2	1.19	0.91	1.50
	Linemen	3	1.42	1.18	1.71
(Savitz et al., 1999)	0-0.6 μT-years	4	1.00	1.00	1.00
	0.6 to < 1.2	5	1.14	1.04	1.26
	1.2 to < 2.0	6	1.19	1.08	1.31
	2.0 to < 4.3	7	1.35	1.22	1.48
	> 4.3	8	1.62	1.45	1.82

TABLE 17.1.1 EPIDEMIOLOGICAL STUDIES OF HEART DISEASE MORTALITY WITH FULL SHIFT MEASUREMENTS OF MAGNETIC FIELDS

REFERENCE	STUDY POPULATION	EXPOSURE METHOD	MAGNETIC FIELD EXPOSURES	CASES	OR (CI)
(Baris et al., 1996a), Cohort mortality study	21,744 Hydro Quebec male utility workers employed an average 12.9 years. Employed between 1970 and 1988. All circulatory disease deaths.	JEMs from 2,066 workweek EMF measurements (50/60 Hz magnetic and electric fields, and pulsed EMF) applied to last job held. Also compared blue-collar and white-collar workers.	< 0.16 μT vs. > 0.16 μT. < 5.76 volts/meter vs. > 5.76 < 23.7 ppm vs. > 23.7 ppm	180 vs. 137 187 vs. 130 249 vs. 68	0.91 (0.73-1.14) 0.76 (0.61-0.95) 0.87 (0.66-1.14)
(Kelsh, 1997) Cohort mortality study	40,335 Southern California Edison utility workers. Mortality determined from 1960-88. SMRs were compared to general population. RRs were also obtained by comparing other utility jobs to administrative staff. Tracked "major cardiovascular" deaths.	Assigned each subject to the job category that he or she had occupied for the longest time while working for the company.	Management/ Professional Service/Labor Linemen Meter Reader/Field Service Plant Operations Trade/Craft Administrative/ Technical Total	103 82 217 25 130 216 223 996	1.19 (0.91-1.5) 1.48 (1.15-1.91) 1.42 (1.18-1.71) 1.71 (1.13-2.58) 1.56 (1.26-1.94) 1.43 (1.19-1.73) 1.00 reference
(Savitz et al., 1999) Cohort mortality study	138,905 men employed for > 6 months in 5 electric utilities, followed for mortality from 1950-86. Deaths due to arrhythmia, acute myocardial infarction, atherosclerosis, and chronic coronary heart disease, examined separately on basis of *a priori* hypothesis from a human experiment by Sastre (Sastre et al., 1998) related to autonomic control of heart rate.	Cumulative magnetic field exposure estimated from job history, plus JEM based on 2841 magnetic field measurements. JEM constructed for 28 occupational categories, collapsed into 5 exposure categories for TWA. Years employed observed for "exposed occupations": electricians, linemen, and power plant operators.	0- 0.6 μT-yrs 0.6-1.2 1.2-< 2.0 2.0-< 4.3 > 4.3 Total	1,031 852 899 946 510 Slope: RR/μT-yr 4,238	1.00 1.14 (1.04-1.26) 1.19 (1.08-1.31) 1.35 (1.22-1.48) 1.62 (1.45-1.82) 1.04 (1.03-1.06)

17.2 ARGUMENTS FOR AND AGAINST CAUSALITY

TABLE 17.2.1

CHANCE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Savitz (Savitz & Loomis, 1995), Baris (Baris et al., 1996a), and Kelsh (Kelsh, 1997) all showed that mortality from heart disease in all utility workers was lower than in the general public.	(F1) The Savitz (Savitz et al., 1999) study has more than 2 million person-years of observation and hundreds of thousands of person-years and hundreds of cases in each exposure category. The probability by chance alone would be extremely small for finding the RR of 1.14 (1.04-1.26) for the next-to-the-lowest exposure category of 6-12 mG-yrs, or for the association reported for the highest category of > 43 mG-yrs (RR = 1.62; CI:1.45-1.82).	(C1) While the RRs are not much above the usual resolution power of typical epidemiological studies, the Savitz (Savitz et al., 1999) study is so large that chance is a vanishingly small explanation of the pattern. This leaves bias, confounding, or causality as possible explanations.
(A2) Baris (Baris et al., 1996a) demonstrated no difference between cardiovascular disease in blue- and white-collar workers or in workers with occupational exposure to high magnetic fields, electric fields, or pulsed electric fields.	(F2) Savitz (Savitz et al., 1999) reanalyzed their data and found that the 65% of deaths due to acute MI or arrhythmia showed a statistically significant, monotonically increasing dose response between mG-yrs of magnetic field exposure and RR. Judging by the confidence intervals, this is very unlikely to be due to chance.	(C2) The healthy worker effect will tend to produce a lower cardiovascular death rate in utility workers as compared to the general population. Savitz (Savitz et al., 1999) had *a priori* reasons to propose that only the acute and arrhythmic infarctions should be sensitive to magnetic fields and the association Savitz demonstrated has not been duplicated elsewhere. It is highly unlikely to be due to chance.

TABLE 17.2.2

BIAS		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Since the relative risks reported by Savitz (Savitz et al., 1999) are less than 2.5, they might be due to bias.	(F1) This study was not subject to selection bias or recall bias. It was subject to measurement bias that, on average, would have biased the associations toward the null.	(C1) No one has invoked a plausible bias to explain this association.

TABLE 17.2.3

CONFOUNDING		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Magnetic field exposure might be associated with other risk factors for cardiovascular death, such as smoking, blood lipids, stress, etc.	(F1) These risk factors do not convey RRs much above the ones observed for magnetic fields. It is not plausible that they could explain away these associations. There are two pieces of evidence which argue against smoking as a plausible confounder. Lung cancer, which is largely driven by smoking, was not associated with magnetic fields in Savitz. Atherosclerotic heart disease is associated with smoking but was not associated with magnetic fields in the Savitz study. The association is limited to acute MI and arrhythmic MI.	(C1) Confounding, while not compelling (there is no reason to suspect that lipid profiles are associated with magnetic fields), has not been ruled out in this study.
(A2) Magnetic field exposure might be confounded with spark and contact current exposure.	(F2) There is not any evidentiary base to link shocks and contact currents to magnetic fields or to heart rate variability.	(C2) One needs to invoke risk factors associated with magnetic field exposure and ONLY sudden and arrhythmic cardiac death. This, too, has not been ruled out.

TABLE 17.2.4

STRENGTH OF ASSOCIATION		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) None of the reported associations are so large that bias or confounding could not be invoked as an alternate explanation	(F1) There are associations with both duration of employment for high exposure groups and μT-yrs of exposure. No specific biases or confounders have been postulated to explain this.	(C1) One is reluctant to discount RRs barely above the resolution power of epidemiological studies routinely if they come from large, well-conducted studies, which is the case with Savitz. This may reflect reality. However, the danger of confounding cannot be ruled out.
	(F2) If exposure misclassification were corrected, the true association might be larger and less vulnerable to bias.	

TABLE 17.2.5

CONSISTENCY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) One should never rely on one study, such as Savitz (Savitz et al., 1999), even if statistically significant.	(F1) Although Savitz (Savitz et al., 1999) may not be fully convincing on its own, the fact that two studies out of three indicate a risk increase is not very likely under the null hypothesis (p = 0.125).	(C1) With only three studies in the literature, consistency is not a very powerful argument for either the null or the alternative hypothesis.

TABLE 17.2.6

HOMOGENEITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) The overall cardiovascular mortality in utility workers is lower than average. In Baris (Baris et al., 1996a), even blue-collar workers had lower than average mortality and no difference as to magnetic field exposure.	(F1) Baris (Baris et al., 1996a) examined all heart disease mortality, while Savitz examined arrhythmic and acute infarction deaths separately. Examining all deaths would have diluted Baris' results. This might explain her null results.	(C1) Kelsh (Kelsh, 1997) and Baris (Baris et al., 1996a) report differing results when examining all cardiovascular deaths, while Savitz reports associations with magnetic fields and with duration of occupation for arrhythmic and acute infarctions.
(A2) If Savitz (Savitz et al., 1999) is right, 65% of these deaths were due to arrhythmic or acute infarctions and the impact of magnetic fields should have been visible.	(F2) Baris dichotomized magnetic field exposure at the median exposure, including persons at risk in the reference group; hence, lessening the chance of seeing an association. Savitz began demonstrating excess risk in the second quintile of exposure. Kelsh (Kelsh, 1997) did see some increased risk for all types of cardiovascular deaths in high magnetic field jobs in the utility industry.	(C2) The smaller studies of Kelsh (36,000 workers) and Baris (22,000 workers) disagree with each other. But Kelsh is compatible with Savitz (139,000 workers).

TABLE 17.2.7

DOSE RESPONSE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) When Baris (Baris et al., 1996a), Kelsh (Kelsh, 1997), and Savitz (Savitz et al., 1999) are taken together, there is no clear dose response.	(F1) Savitz (Savitz et al., 1999) defines disease differently and is much larger than the other two. The 376, 625, and 507 acute myocardial infarctions, respectively, in electricians, linemen and power plant operators show an orderly increase of risk with increasing duration of employment; and the 4238 acute myocardial infarctions show an orderly increase in risk with increasing mG-years of exposure.	(C1) The only study to examine the subset of heart disease that is believed to be sensitive to the governance of the conduction system, acute myocardial infarction, shows an orderly dose response in three independent high-exposure jobs within the utility industry.
(A2) Kelsh (Kelsh, 1997) shows higher cardiovascular mortality for a variety of jobs, but the greatest RRs are not for the jobs that are the most highly exposed, linemen and plant operators.	(F2) Kelsh's job categories are quite broad and may have obscured differences.	(C2) RR/μT–yr = 1.04 (1.03-1.06).

TABLE 17.2.8

COHERENCE/VISIBILITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) A dramatic increase in cardiovascular death should have been seen when electricity was introduced and, afterward, as electricity use increased.	(F1) Before electrification, there was virtually no accumulated exposure. Now 75% of the population has a 24-hour TWA of .7 mG or more and would accumulate at least 49 mG-years over a 70-year lifetime. The data from Savitz suggests that a subset of CHD deaths would have increased by a factor of 1.41. The reviewers calculate that the total CHD rate might have increased by a factor of 1.21. This is not a dramatic change within the context of the change in dietary and other risk factors over the 20th century.	(C1) The Savitz (Savitz et al., 1999) data suggest the possibility that residential and occupational exposures could accumulate to produce epidemiologically detectable effects, yet these would not have dramatically changed overall CHD death rates.
	(F2) The coherence of dose response in three independent occupations in the Savitz (Savitz et al., 1999) utility study commands attention.	(C2) The internal coherence of the Savitz findings with regard to duration of employment and risk in three high-exposure jobs, and the association with mG-years for various lag times, increases the confidence somewhat.

TABLE 17.2.9

EXPERIMENTAL EVIDENCE		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) There is only one study showing an effect on heart rate variability (Sastre et al., 1998), and a replication study had not been reported by June 2000, the deadline for this evaluation.	(F1) Sastre (Sastre et al., 1998) showed an effect of 200 mG on heart rate variability in humans. Decreased heart rate variability has been associated with increased risk of cardiac events (Tsuji et al., 1996), (Martin, 1987).	(C1) The experimental evidence is scanty but suggestive.
	(F2) Various experimental results of bioeffects at high levels of EMF increase the credibility of the hypothesis that EMFs may interfere with living organisms.	

TABLE 17.2.10

PLAUSIBILITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Even if EMFs produced transient effects on heart rate variability, the mechanism for long term exposures would have no theoretical basis.	(F1) Continual perturbation of the autonomic control of cardiac rhythm might produce permanent changes	(C1) The evidentiary base is scanty and insufficient to support or refute hypotheses.

TABLE 17.2.11

ANALOGY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
	NA	NA

TABLE 17.2.12

TEMPORALITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Not an issue.	(F1) Not an issue.	(C1) Not an issue.

TABLE 17.2.13

SPECIFICITY		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Death certificate diagnoses are not reliable; the rationale for separating arrhythmic and acute infarctions from other infarctions or cardiac deaths is not very compelling.	(F1) The *a priori* specification of death certificate rubrics produced the predicted differential effect of mG-yrs of exposure.	(C1) The *a priori* predicted effect on a subset of CHD deaths increases confidence somewhat.
	(F2) The non-differential misclassification of disease and exposure should not have produced the kind of orderly dose response seen in the Savitz study.	

TABLE 17.2.14

OTHER DISEASE ASSOCIATIONS		
AGAINST CAUSALITY	**FOR CAUSALITY**	**COMMENT AND SUMMARY**
(A1) Statistical associations with cancers, miscarriage, or ALS should not be relevant to associations with CHD mortality.	(F1) While these diseases have different etiologies, the ability to cause one disease should boost the credibility of EMFs causing other diseases.	(C1) The associations with other diseases have some effect.

TABLE 17.2.15

SUMMARY TABLE FOR HEART DISEASE			
	HOW LIKELY IS THIS ATTRIBUTE OF THE EVIDENCE UNDER:		
ATTRIBUTE OF THE EVIDENCE	**"NO-EFFECT" HYPOTHESIS**	**CAUSAL HYPOTHESIS**	**HOW MUCH AND IN WHAT DIRECTION DOES THIS ATTRIBUTE CHANGE CERTAINTY?**
Chance: highly unlikely.	Unlikely		Increase
Upward bias: not suggested.	Possible	Possible	No impact
Confounding: a remote possibility.	More possible	Possible	No impact or slight decrease
Combination of bias, confounding and chance	More Possible	Possible	Slight decrease
Strength of association: does not exceed plausible confounding or bias.	More possible	Possible	No impact or slight decrease
Consistency: two studies out of three indicate a risk.	Possible	Possible	No effect
Homogeneity: Baris's results appear to be inconsistent with others.	More possible	Possible	No impact or slight decrease
Dose response: monotonic for duration and μ-T years in a large study.	Unlikely	Likely	Substantial Increase
Coherence: in several jobs and predicted invisibility in national rates.	Unlikely	Possible	Slight Increase
Experimental evidence: in Sastre study.	Possible	More possible	No impact or slight increase
Plausibility: lack of strong mechanistic explanation.	Possible	Possible	None
Analogy.	Possible	Possible	None
Temporality: not a problem.	Possible	Possible	None
Specificity of association: with arrhythmia's and acute MI. Other disease associations.	Possible	More possible	No impact or slight increase
Only one study shows orderly association.	More possible	Possible	No impact to substantial decrease

17.3 IARC CLASSIFICATION AND CERTAINTY OF CAUSALITY

17.3.1 STATEMENTS OF INDIVIDUAL REVIEWERS

REVIEWER 1 (DELPIZZO)

Degree of Certainty: With two smaller studies suggesting opposite conclusions, the evaluation is based on a single, though very large, study. The prior is boosted by a very clear monotonic dose-response relationship. In the opinion of Reviewer 1, the combined pattern of evidence is considerably more likely to occur if the association is causal than if EMFs were really harmless. Reviewer 1 is "close to the dividing line between believing and not believing." He has a confidence range of 25 to 55 and a median value of 42.

IARC Classification: Inadequate evidence.

REVIEWER 2 (NEUTRA)

Degree of Certainty: A small, human experiment (Sastre et al., 1998), unreplicated by deadline for this evaluation (June 2000), suggests that EMFs might affect autonomic control of heart rate in a way that might increase the risk of sudden cardiac death. This hypothesis is tested in a very large, state-of-the-art, retrospective cohort study by Savitz (Savitz et al., 1999). It shows a monotonic dose response with tight confidence intervals for duration of work in highly exposed workers, but for μT-years of exposure, only for the hypothesized subtypes of cardiac mortality, arrhythmic deaths and acute myocardial infarction. Overall, cardiac mortality is lower than the general population, as expected for healthy workers. The more routine comparison of total cardiac mortality showed no increased mortality in one study by Baris (Baris et al., 1996a). The Baris study compared all cardiac deaths in persons above and below the median and may have been too crude a comparison, which may well mask an effect in the upper few percent of the exposure distribution. Another study by Kelsh (Kelsh, 1997) showed some differences between exposed and unexposed occupations for all cardiac deaths combined.

All of these studies are state-of-the-art occupational mortality studies, with careful job exposure matrices. The very large Savitz study was the only one analyzed so as to specifically address the autonomic hypothesis. Its specificity, coherence, monotonic dose response, and statistical precision all go to provide a pattern of evidence extremely unlikely to be due to chance. But it is only one study. Could there be a confounder? State-of-the-art retrospective occupational cohort studies, such as this one, have not been able to collect confounding information on the subjects. Heart disease is a well-studied endpoint and there are many recognized risk factors. Smoking is an unlikely confounder, since lung cancer and atherosclerotic heart disease (strongly determined by smoking) were not associated with magnetic field exposure in the Savitz study. Shocks or contact currents, or other aspects of the EMF mixture, cannot be ruled out but have little supportive evidence.

Any confounder would have to be specifically related to arrhythmic and sudden cardiac death but not to other heart disease deaths. Other than non-differential exposure misclassification, which on average would tend to underestimate risk but could rarely increase apparent risk in a single study, bias seems unlikely. The good quality and very large size of the Savitz study makes chance an extremely unlikely explanation of its findings, but Reviewer 2's degree of certainty was pulled down by there being only one really relevant study and by the possibility of confounding.

Despite this, Reviewer 2 was moved by the evidence above the prior degree of certainty. Given the reviewer's initial degree of certainty for the range of effect that contains what has subsequently been observed, and all the streams of evidence, this reviewer has a posterior degree of certainty which one could characterize as "prone not to believe" that EMFs can increase the risk of heart attack. On a scale from 0 to 100, he has a wide range of uncertainty from 8 to 60 and a median estimate of 30. This is the degree of certainty that something about the EMF mixture, probably magnetic fields, is related to arrhythmic or acute myocardial infarction.

IARC Classification: Because there is only one study that properly analyzes the data and because there is no relevant animal experimental evidentiary base or strong mechanistic evidentiary base, Reviewer 2 would classify the heart disease evidence with an IARC classification of "inadequate" evidence to associate EMFs with arrhythmic or acute myocardial death.

REVIEWER 3 (LEE)

The human evidence of the heart disease studies are based on three studies, all occupation mortality studies, where only one study was large enough to assess a dose response and subtypes (Savitz et al., 1999). One study (Baris et al., 1996a) found no excess cardiovascular mortality. Overall, the consistent increased apparent risk just above the resolution power of two studies, as well as the evidence of a dose response, increases Reviewer 3's posterior above the prior. The fact that

confounding and other biases are a possible explanation and that only three studies contribute to the body of evidence decreases the posterior somewhat. Hence, the posterior degree of certainty for purposes of the policy analysis falls within the "prone not to believe" that EMFs increase the risk of heart attack to any degree. The degree of certainty centers around 25, with a range of 10 to 55

IARC Classification: The human evidence is weak, since it is based on three studies with only one sufficiently large study. Hence, chance, bias, and confounding cannot be ruled out. Also, the animal evidence is lacking, and there is no sound mechanistic rationale. Given this, the evidence as a whole is sufficient for a classification of "inadequate" evidence.

17.3.2 SUMMARY OF THE THREE REVIEWERS' CLASSIFICATIONS

CONDITION	REVIE-WER	IARC CLASS	CERTAINTY PHRASE	DEGREE OF CERTAINTY FOR POLICY ANALYSIS THAT AN AGENT (EMFs) INCREASES DISEASE RISK TO SOME DEGREE
Heart Disease				0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100
	1	3	Close to dividing line	
	2	3	Prone not to believe	
	3	3	Prone not to believe	

17.4 QUESTIONS RELEVANT TO DOSE AND THE STATE OF THE SCIENCE

The following tables deal with evidence relevant to potentially bioactive aspects of the EMF mixture, the shape of dose-response curves (if any), evidence for unfair vulnerability or exposure (if any), and the state of the science.

TABLE 17.4.1

HOW CONFIDENT ARE THE REVIEWERS THAT SPECIFIC EXPOSURE METRIC OR ASPECT OTHER THAN 60 HZ TWA MAGNETIC FIELD IS ASSOCIATED WITH THIS DISEASE?	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Magnetic fields might be confounded with shocks and contact currents. (C2) An elaborate job exposure matrix suggests that accumulated mG-years are predictive of risk. (C3) Long-term magnetic field exposure seems associated with risk. One cannot guarantee that a non-EMF confounder or another metric might be responsible for the association.	(I1) Some possibility that mitigating TWA would not affect risk.

TABLE 17.4.2

EVIDENCE FOR THRESHOLD OR PLATEAU	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) No evidence suggesting a threshold. (C2) The effect of work-time exposure may add to the effect of other exposures. Averaging time may be shorter than 24 hours, so that "hits" at home add to "hits" at work. (C3) The data from Savitz suggest an association with 6-12 mG-years, within 5 years of exposure. Many occupations and residential settings could accumulate this kind of mG-year exposure.	(I1) If causal, these associations would affect a large proportion of population and could produce effects of regulatory concern.

TABLE 17.4.3

EVIDENCE FOR BIOLOGICAL WINDOWS OF VULNERABILITY	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) These are primarily daytime exposures. Not much is known about nighttime exposures. (C2) Not particularly helpful in demonstrating biological windows of vulnerability.	No impact.

TABLE 17.4.4

CONSISTENT INDUCTION PERIOD OR REQUIRED DURATION OF EXPOSURE	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Durations longer than 10 years and incubations as short as 5 years show associations in the Savitz (Savitz et al., 1999) study. (C2) The large numbers in the Savitz (Savitz et al., 1999) study allowed exploration of these issues. One sees stronger associations with longer exposure and effects within 5 years of the cessation of exposure.	(I1) If true, suggests that effects can show up within 5 years and can persist, and that prolonged exposure might increase risk. Could be relevant to work assignments and land use.

TABLE 17.4.5

EMFS COMPARED TO OTHER RISK FACTORS FOR THIS DISEASE	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) In the same ballpark as some of the recognized moderate risk factors. (C2) This is more relevant to risk perception than policy. Utilitarian policy is driven by the cost effectiveness of mitigation, not the effect relative to the effect of other factors.	No impact.

TABLE 17.4.6

RELATIVE RISK COMPARED TO THAT WHICH WOULD GENERATE 1/1,000 OR 1/100,000 THEORETICAL LIFETIME RISK	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) The average incidence of heart disease mortality is about 1/1,000, a 1.14 fold increase (the RR conveyed by the lowest Savitz exposure category sustained for 20 to 40 years of residence or occupation) would be more than the occupational regulatory benchmark of 1/1000 added lifetime risk or the environmental benchmark of 1/100,000. (C2) If true, these associations would convey lifetime theoretical risks of regulatory interest. (C3) There are about 17,000 sudden cardiac deaths in California each year. Even if EMFs accounted for only a few percent of these, the attributable cases would be in the hundreds per year because of this being a common event.	(I1) If true, could be of regulatory concern.

TABLE 17.4.7

EVIDENCE FOR RACIAL OR CLASS DIFFERENCES IN EXPOSURE OR VULNERABILITY	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
No evidentiary base.	No impact.

TABLE 17.4.8

ROOM FOR IMPROVEMENT IN QUALITY OR SIZE IN BEST EXISTING STUDIES	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Savitz (Savitz et al., 1999) did not control for confounding. (C2) Confounders not likely to explain associations. (C3) One is reluctant to base policy on one study, but in a study this large, controlling for confounding is unlikely to be done.	(I1) Raises issue of how to verify large well-done study.

TABLE 17.4.9

NEW STUDIES IN PIPELINE AND THEIR ABILITY TO RESOLVE ISSUE	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Re-analysis of the Kelsh (Kelsh, 1997) study and the Harrington (Harrington et al., 1997) study are underway. (C2) Kelsh-Sahl was one-quarter the size and Harrington was not much more than half the size of the Savitz (Savitz et al., 1999) study. They are unlikely to resolve this issue. (C3) If the Kelsh and Harrington studies confirmed the findings, they could strengthen the reviewers' conviction; if they do not, they would not cancel out Savitz. (C4) Nothing is now planned that would be likely to resolve this issue. (C5) A study by Graham (Graham, Cook & Sastre, 2000) came out after the June 2000 deadline. It did not confirm the Sastre (Sastre et al., 1998) experiment. The authors proposed testable reasons for these inconsistent results.	(I1) Will have some weight on interim actions and substantial weight on research directions.

TABLE 17.4.10

HOW LIKELY IS IT THAT FURTHER STUDIES COULD RESOLVE CONTROVERSIES?	
COMMENT AND SUMMARY	**IMPACT ON POLICY**
(C1) Experiments using individual aspects of the EMF mixture may not be sensitive tests for the effect of the mixture itself. (C2) Experiments using actual environmental exposures may have a role. (C3) Job Exposure Matrix studies dealing with magnetic fields, electric fields, contact currents, shocks, and various summary exposure metrics will be needed to deal with suspected confounding with magnetic fields. (C4) Very large cohort studies or case-control studies are needed with refined diagnosis and sufficient numbers of highly exposed subjects. It would be helpful to explore supplementing existing CHD studies with occupational and residential histories. In cohort studies, prospective ascertainment of appliance use would be possible. (C5) Non-utility worker EMF exposures are likely to have different confounders than utility worker exposures, so that coherent results in other populations would increase confidence considerably and lack of confirmation would decrease it considerably.	(I1) The frequency of sudden cardiac death is so great that it is cost-beneficial to investigate it. (I2) The reported incubation period is short enough that this endpoint lends itself to study.

17.5 Conclusions About Dose and The State of the Science

17.5.1 Dose-Response Issues

Magnetic field exposure, or something associated with it, may influence acute MI deaths. The evidentiary base does not allow conclusions about which aspect of the mixture. The lower quintile categories of μT-years in workers overlaps with μT-years expected from residential exposures, but it is difficult to extrapolate to the general population.

The relative risks conveyed by these lower quintiles, if real, would translate to theoretical added lifetime risks above the 1/100,000 and 1/1,000 benchmarks that trigger regulatory action in the domain of carcinogens. Even if EMFs accounted for only a few percent of the 17,000 annual sudden cardiac deaths in California, this would be equivalent to hundreds of deaths per year. As years of exposure increase, the association becomes stronger. The data support a lag period of as short as 5 years.

17.5.2 Research Policy

An experiment by Graham (Graham et al., 2000), which came out after the deadline, does not confirm Sastre (Sastre et al., 1998). The re-analyses in the pipeline are of studies substantially smaller than the Savitz (Savitz et al., 1999) study. If they show similar results they would increase confidence; if they disagree they would not have the weight to cancel Savitz. For a common condition such as acute myocardial infarction, the value of information is high. Experimental studies and re-analysis of epidemiological studies should receive the highest research priority.